



4164-01-P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA-2010-N-0117]

Agency Information Collection Activities; Submission for Office of Management and Budget Review; Comment Request; Guidance for Industry on Hypertension Indication: Drug Labeling for Cardiovascular Outcome Claims

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA or we) is announcing that a proposed collection of information has been submitted to the Office of Management and Budget (OMB) for review and clearance under the Paperwork Reduction Act of 1995 (the PRA).

DATES: Fax written comments on the collection of information by [INSERT DATE 30 DAYS AFTER DATE OF PUBLICATION IN THE FEDERAL REGISTER].

ADDRESSES: To ensure that comments on the information collection are received, OMB recommends that written comments be faxed to the Office of Information and Regulatory Affairs, OMB, Attn: FDA Desk Officer, FAX: 202-395-7285, or emailed to oir_submission@omb.eop.gov. All comments should be identified with the OMB control number 0910-0670. Also include the FDA docket number found in brackets in the heading of this document.

Guidance for Industry on Hypertension Indication: Drug Labeling for Cardiovascular
Outcome Claims

OMB Control Number 0910-0670--Extension

This guidance is intended to assist applicants in developing labeling for outcome claims for drugs that are indicated to treat hypertension. With few exceptions, current labeling for antihypertensive drugs includes only the information that these drugs are indicated to reduce blood pressure; the labeling does not include information on the clinical benefits related to cardiovascular outcomes expected from such blood pressure reduction. However, blood pressure control is well established as beneficial in preventing serious cardiovascular events, and inadequate treatment of hypertension is acknowledged as a significant public health problem. FDA believes that the appropriate use of these drugs can be encouraged by making the connection between lower blood pressure and improved cardiovascular outcomes more explicit in labeling. The intent of the guidance is to provide common labeling for antihypertensive drugs except where differences are clearly supported by clinical data. The guidance encourages applicants to submit labeling supplements containing the new language.

The guidance contains two provisions that are subject to OMB review and approval under the PRA and one provision that would be exempt from OMB review:

1. Section IV.C of the guidance requests that the CLINICAL STUDIES section of the Full Prescribing Information of the labeling should include a summary of placebo or active-controlled trials showing evidence of the specific drug's effectiveness in lowering blood pressure. If trials demonstrating cardiovascular outcome benefits exist, those trials also should be summarized in this section. Table 1 in Section V of the guidance contains the specific drugs for which FDA has

concluded that such trials exist. If there are no cardiovascular outcome data to cite, one of the following two paragraphs should appear:

“There are no trials of [DRUGNAME] or members of the [name of pharmacologic class] pharmacologic class demonstrating reductions in cardiovascular risk in patients with hypertension,” or “There are no trials of [DRUGNAME] demonstrating reductions in cardiovascular risk in patients with hypertension, but at least one pharmacologically similar drug has demonstrated such benefits.”

In the latter case, the applicant's submission generally should refer to table 1 in section V of the guidance. If the applicant believes that table 1 is incomplete, it should submit the clinical evidence for the additional information to Docket No. FDA-2008-D-0150. The labeling submission should reference the submission to the docket. FDA estimates that no more than one submission to the docket will be made annually from one company, and that each submission will take approximately 10 hours to prepare and submit. Concerning the recommendations for the CLINICAL STUDIES section of the Full Prescribing Information of the labeling, FDA regulations at §§ 201.56 and 201.57 (21 CFR 201.56 and 201.57) require such labeling, and the information collection associated with these regulations is approved by OMB under OMB control number 0910-0572.

2. Section VI.B of the guidance requests that the format of cardiovascular outcome claim prior approval supplements submitted to FDA under the guidance should include the following information:

- A statement that the submission is a cardiovascular outcome claim supplement, with reference to the guidance and related Docket No. FDA-2008-D-0150.
- Applicable FDA forms (e.g., 356h, 3397).

- Detailed table of contents.
- Revised labeling to:
 - Include draft revised labeling conforming to the requirements in §§ 201.56 and 201.57 and
 - include marked-up copy of the latest approved labeling, showing all additions and deletions, with annotations of where supporting data (if applicable) are located in the submission.

FDA estimates that approximately 1 cardiovascular outcome claim supplement will be submitted annually from approximately 1 different companies, and that each supplement will take approximately 20 hours to prepare and submit. The guidance also recommends that other labeling changes (e.g., the addition of adverse event data) should be minimized and provided in separate supplements, and that the revision of labeling to conform to §§ 201.56 and 201.57 may require substantial revision to the ADVERSE REACTIONS or other labeling sections.

3. Section VI.C of the guidance states that applicants are encouraged to include the following statement in promotional materials for the drug.

“[DRUGNAME] reduces blood pressure, which reduces the risk of fatal and nonfatal cardiovascular events, primarily strokes and myocardial infarctions. Control of high blood pressure should be part of comprehensive cardiovascular risk management, including, as appropriate, lipid control, diabetes management, antithrombotic therapy, smoking cessation, exercise, and limited sodium intake. Many patients will require more than one drug to achieve blood pressure goals.”

The inclusion of this statement in the promotional materials for the drug would be exempt from OMB review based on 5 CFR 1320.3(c)(2), which states that the public disclosure of

information originally supplied by the Federal government to the recipient for the purpose of disclosure to the public is not included within the definition of collection of information.

In the Federal Register of February 22, 2016 (81 FR 8726), we published a 60-day notice requesting public comment on the proposed extension of this collection of information. No comments were received.

We estimate the burden of this collection of information as follows:

Table 1.--Estimated Annual Reporting Burden¹

Activity	No. of Respondents	No. of Responses per Respondent	Total Annual Responses	Hours Per Response	Total Hours
Submission to Docket No. FDA-2008-D-0150	1	1	1	10	10
Cardiovascular Outcome Claim Supplement Submission	1	1	1	20	20
Total					30

¹ There are no capital costs or operating and maintenance costs associated with this collection of information.

Dated: October 27, 2016.

Leslie Kux,

Associate Commissioner for Policy.

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